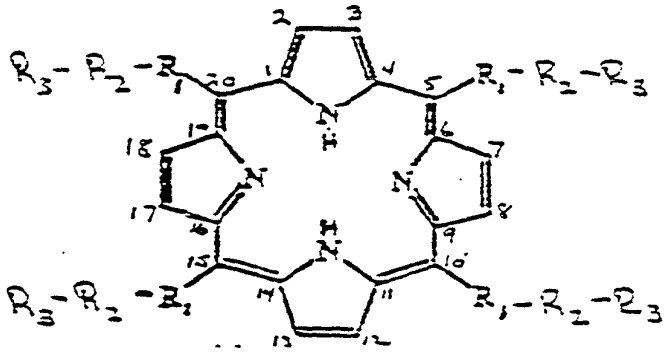
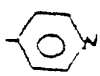
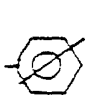
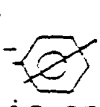
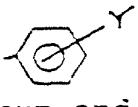


or a pharmaceutically acceptable salt thereof,

wherein:

R_1 is a bond -  ,  ,  ,

 ,  ,  ,  , or 

wherein X is a halogen and Y is an alkyl group and

wherein  indicates bonding to R_2 at any position and  indicates bonding to R_2 and the substituent at any position; and

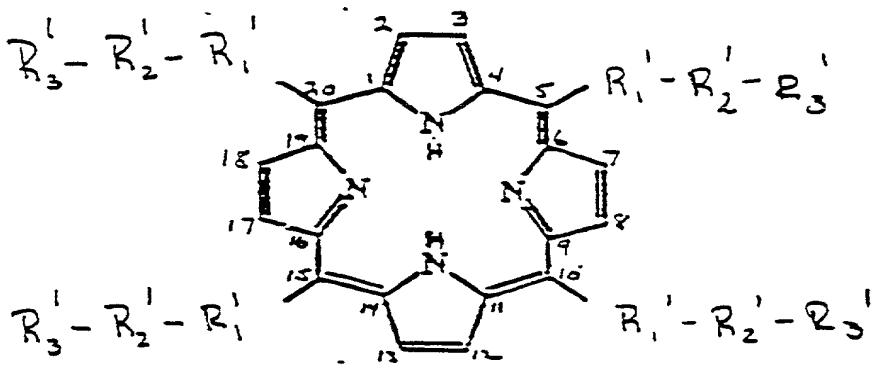
R_2 is a bond, $-(CY'_2)_n-$, $-(CY'_2-CY'=CY')_n-$,

$-(CY'_2-CY'_2-CH=CH)_n-$, $-(CY'=CY')_n-$, or $-(CY'_2-\overset{O}{\overset{\|}{C}})_n-$,

wherein Y' is hydrogen or an alkyl group and wherein n is 1 to 8; and

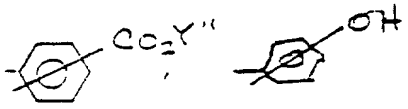
R_3 is -Y", -OH, $-NH_2$, $-N^+(Y")_3$, -COOH, $-COO^-$, $-SO_3H$, $-SO_3^-$, $-C-PO_3H_2$ or $-C-PO_3H^-$, wherein Y" is an alkyl group.

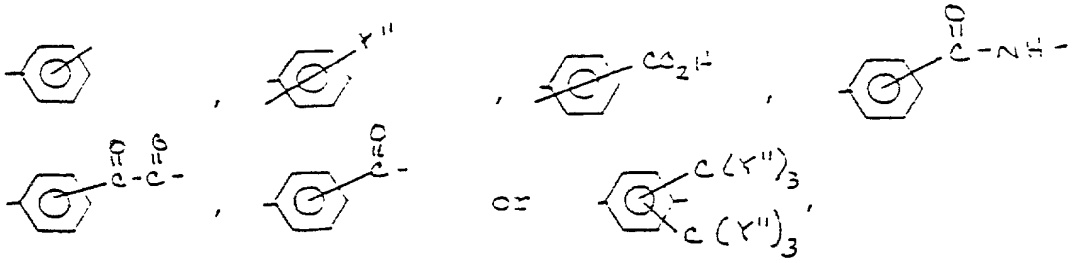
Fig. 1A



or a pharmaceutically acceptable salt thereof,

wherein:

each R_1' is independently a bond, 



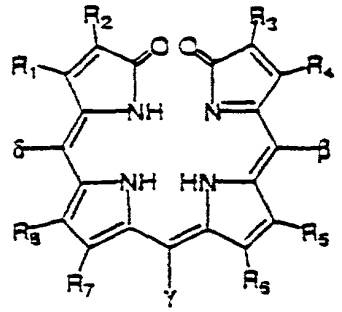
wherein Y" is an alkyl group, and wherein  indicates bonding to R_2' at any position and  indicates bonding to R_2' and the R_1' phenyl substituent at any position;

each R_2' is independently a bond, or $-(CH_2)_n-$ wherein n is 1-4,

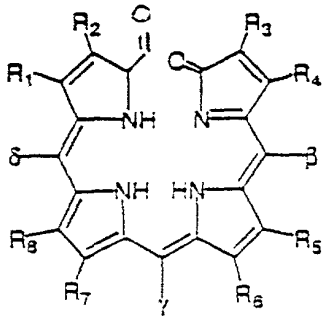
each R_3' is independently -Y", -Y'", -H, -OH, -OY", $-NO_2$, -CN, $-NH_2$, -COOH, -COY", $-COO^-$, or a heterocyclic group, wherein Y" is as defined above and Y'" is a primary, secondary, tertiary or quaternary amine.

Fig. 1B.

Fig. 1C



I



II

R_1 through R_8 are, independently, -H, alkyl, 2-hydroxyalkyl, methoxyalkyl, halogen, nitro, cyano, trialkylammonium, formyl, amide of carboxylic acid, alkyl ester of carboxylic acid, carboxylic acid, glucuronyl or glyceryl ester of carboxylic acid, 1,2-dihydroxyalkyl, acetyl, vinyl, glycosyl or, taurate, and

β, γ and δ are, independently, -H, acetyl, glycyl, benzoate, phenylsulfonate, 2-, or 3-, or 4-N-alkyl-pyridyl, nitrophenyl, halophenyl, methoxyalkyl, halogen, nitro, cyano, trialkylammonium, formyl, amide of carboxylic acid.

Fig 1D

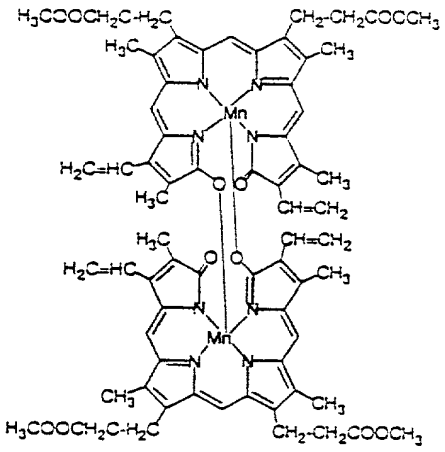
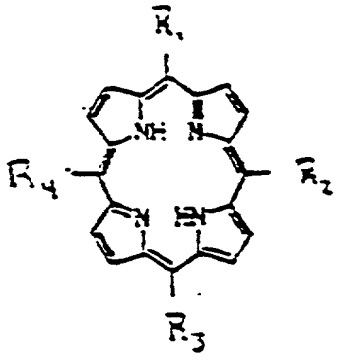

H3COOCH2C-H2C
CH2-CH2COOCH3
H3C
CH3
Mn
H2C=HC
CH3
H3C
CH=CH2
O
O
Mn
CH3
H3COOCH2C-H2C
CH2-CH2COOCH3

Fig. 1E

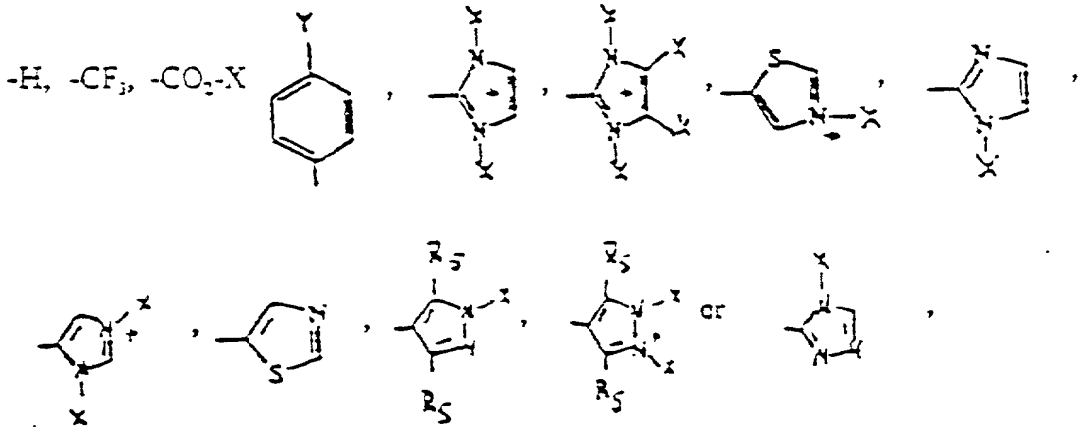


I

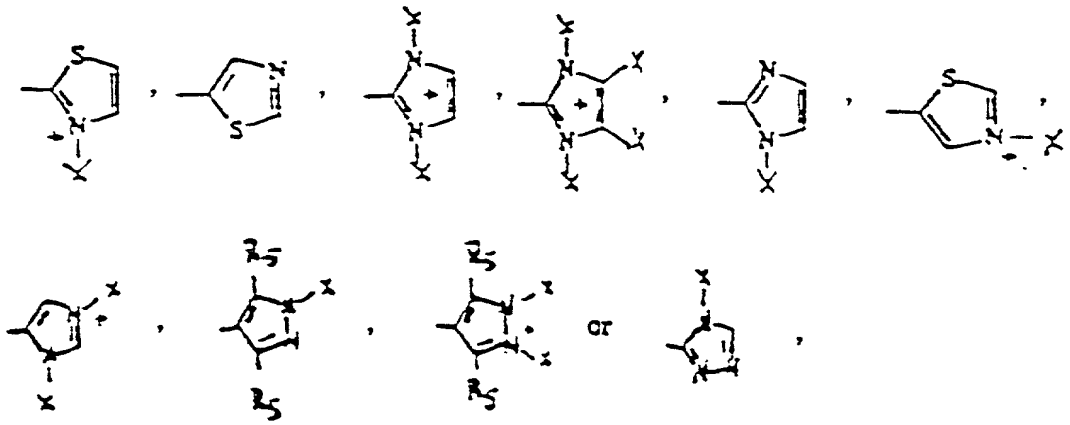
or pharmaceutically acceptable salt thereof

wherein:

R_1 and R_3 are the same and are:



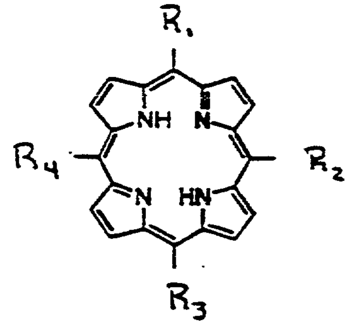
R_2 and R_4 are the same and are :



Y is halogen or $-CO_2X$,

each X is the same or different and is an alkyl and each R_5 is the same or different (preferably the same) and is H or alkyl.

Fig 1F



I

or pharmaceutically acceptable salt thereof

wherein:

R_1 and R_3 are, independently:

$-CO_2C_{1-4}$ alkyl; or

$-CO_2(CH_2)_nCX_3$, wherein X is halogen and n = 1 to 3;

R_2 is:

-H

$-C_{1-4}$alkyl

-COOH

$-CO_2C_{1-4}$ alkyl,

$-CO_2(CH_2)_nCX_3$, wherein X is halogen and n = 1 to 3,

$-CON(CH_3)_2$, or

$-CX_3$, wherein X is halogen; and

R_4 is:

-H,

$-C_{1-4}$alkyl

-COOH,

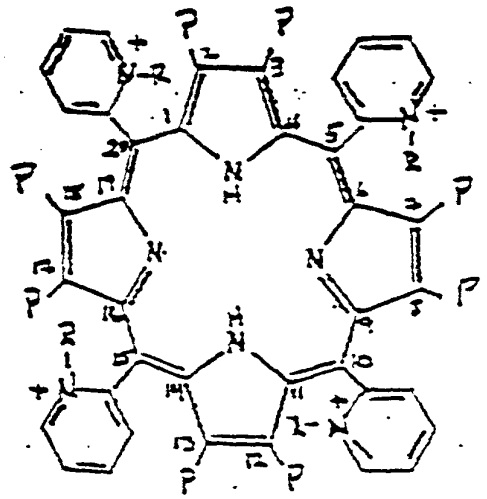
$-CO_2C_{1-4}$ alkyl,

$-CO_2(CH_2)_nCX_3$, wherein X is halogen and n = 1 to 3,

$-CON(CH_3)_2$, or

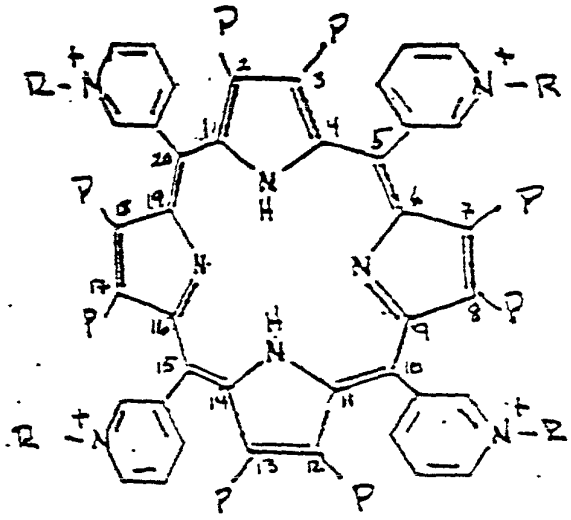
$-CX_3$, wherein X is halogen.

Fig 1G



I

or



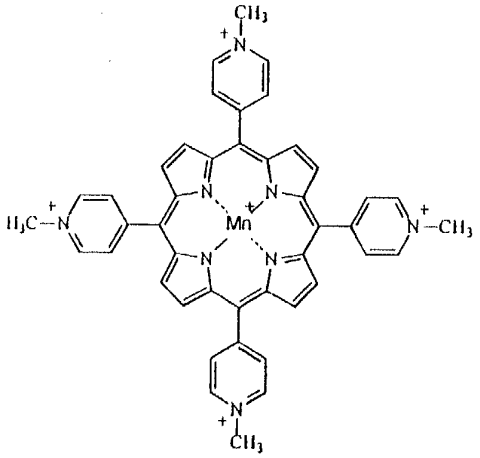
II,

or pharmaceutically acceptable salt thereof,

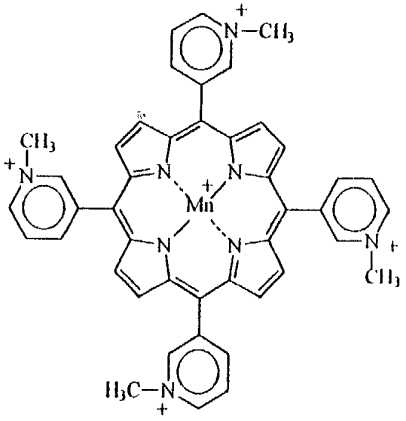
wherein

each R is, independently, a C_1-C_8 alkyl group, and

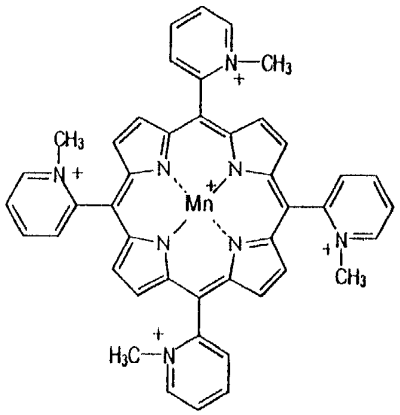
each P is, independently, an electron withdrawing group or hydrogen.



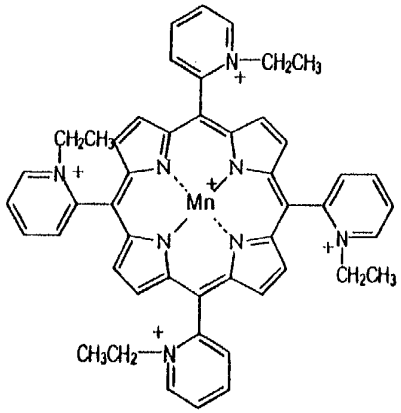
10110
MnTM-4-PyP



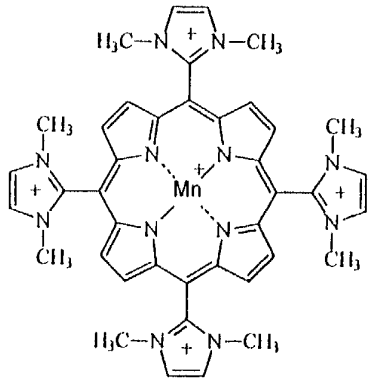
10111
MnTM-3-PyP



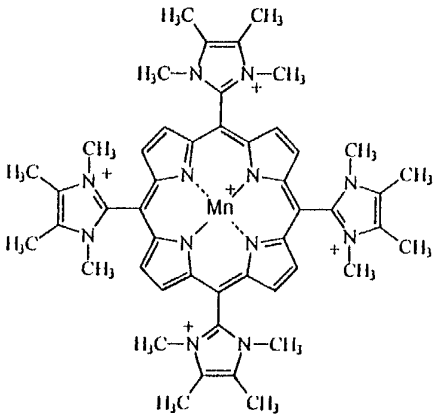
10112
MnTM-2-PyP



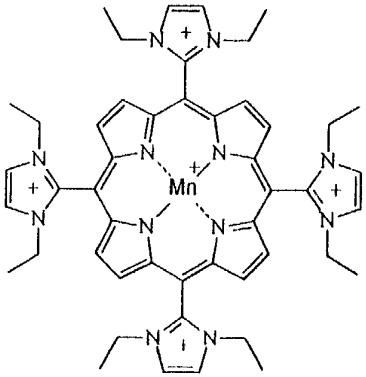
10113
MnTE-2-PyP



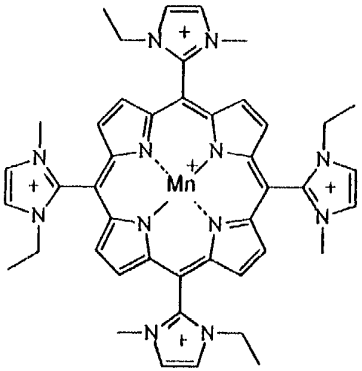
10123
MnTDM-2,5-IP



10143

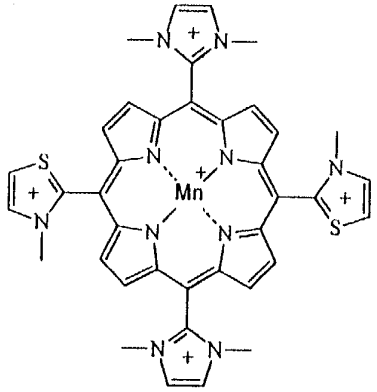


10150
MnTDE-2,5-IP

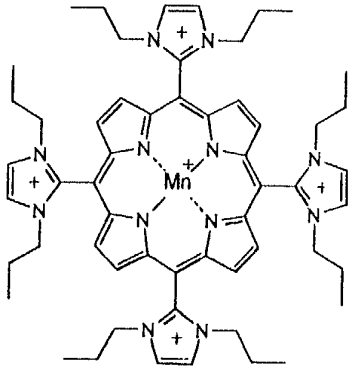


10151

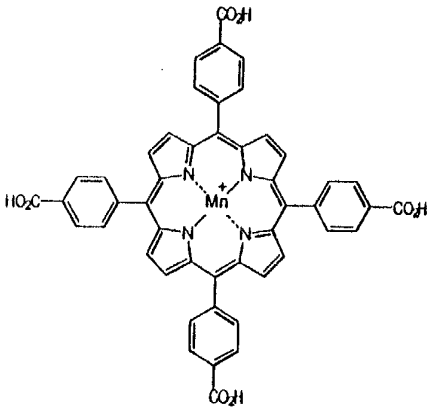
Fig. 1H continued



10153



10158
MnTDP-2,5-IP



10201
MnTBAP

Figure 2A

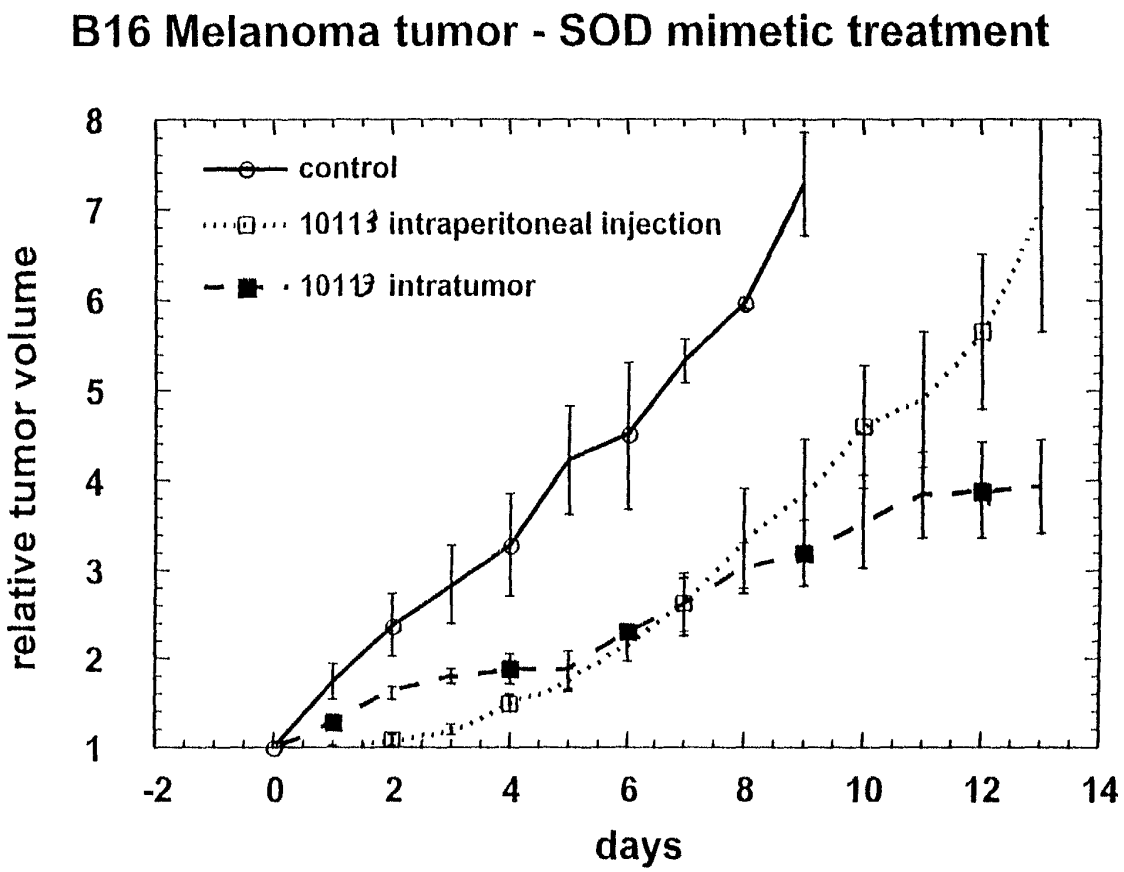
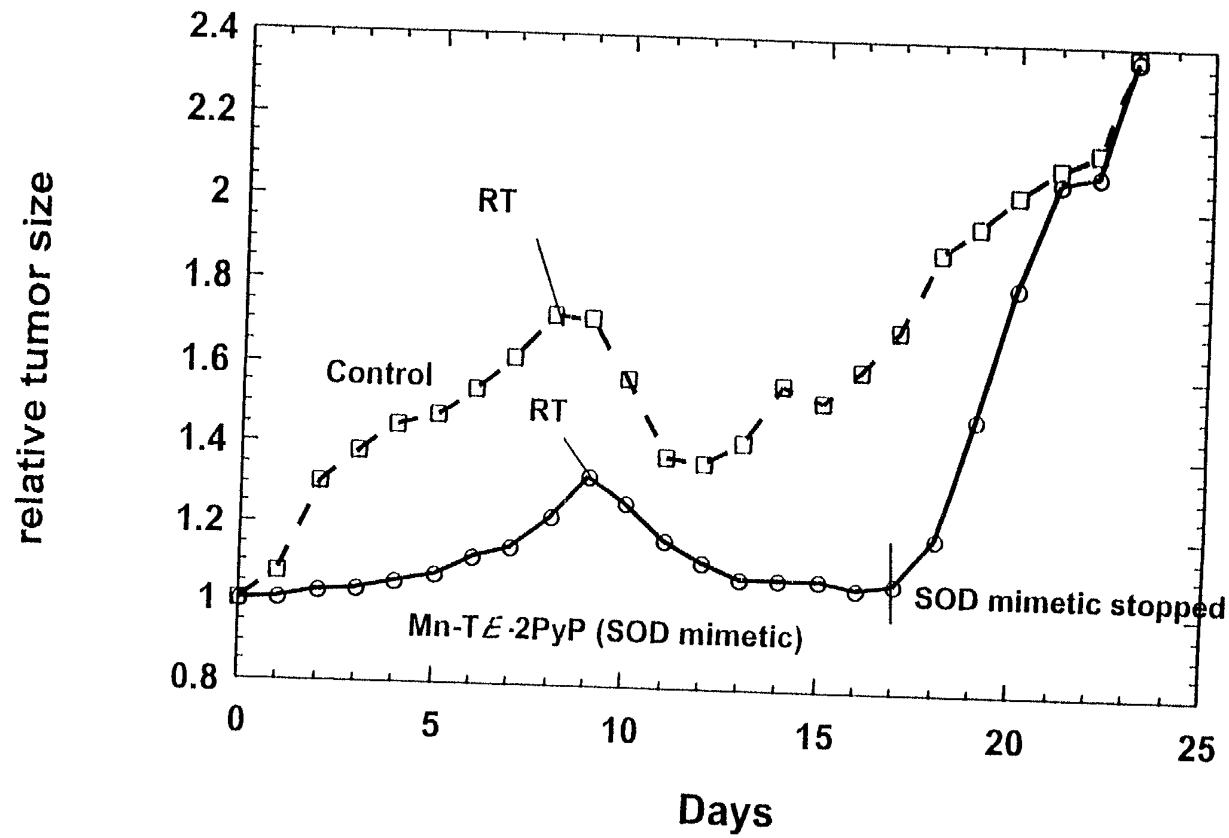


Figure 2B


relative tumor size
2.4
2.2
2
1.8
1.6
1.4
1.2
1
0.8
0
5
10
15
20
25
Days
Control
RT
RT
Mn-TE-2PyP (SOD mimetic)
SOD mimetic stopped

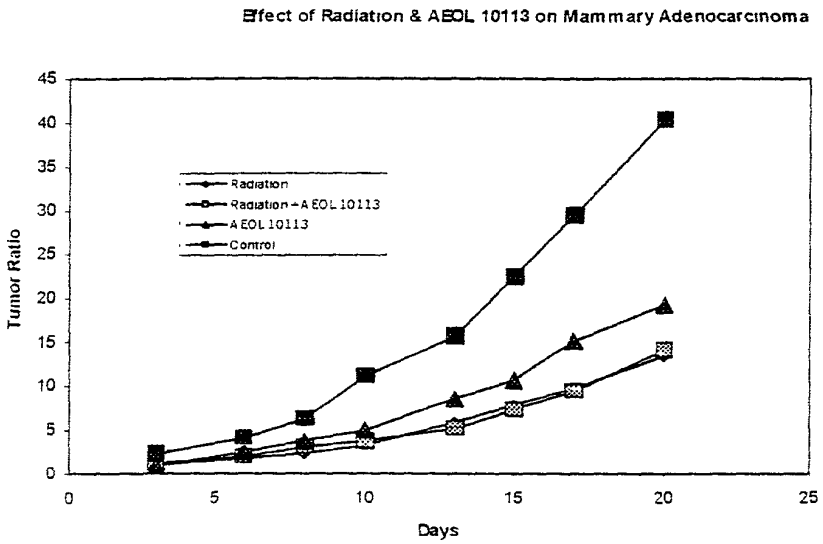


Fig 2C

Figure 3

Tumor Growth Inhibition
R3230 AC Mammary Adenocarcinoma in Fisher rats

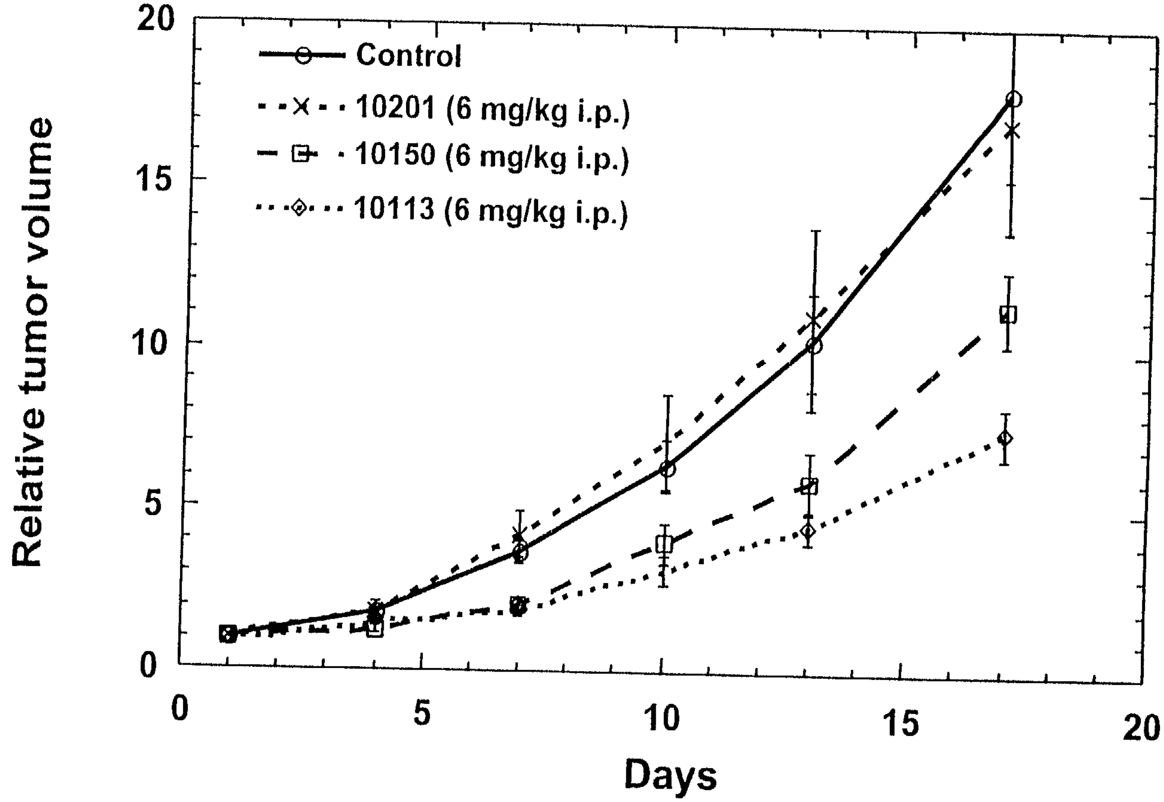
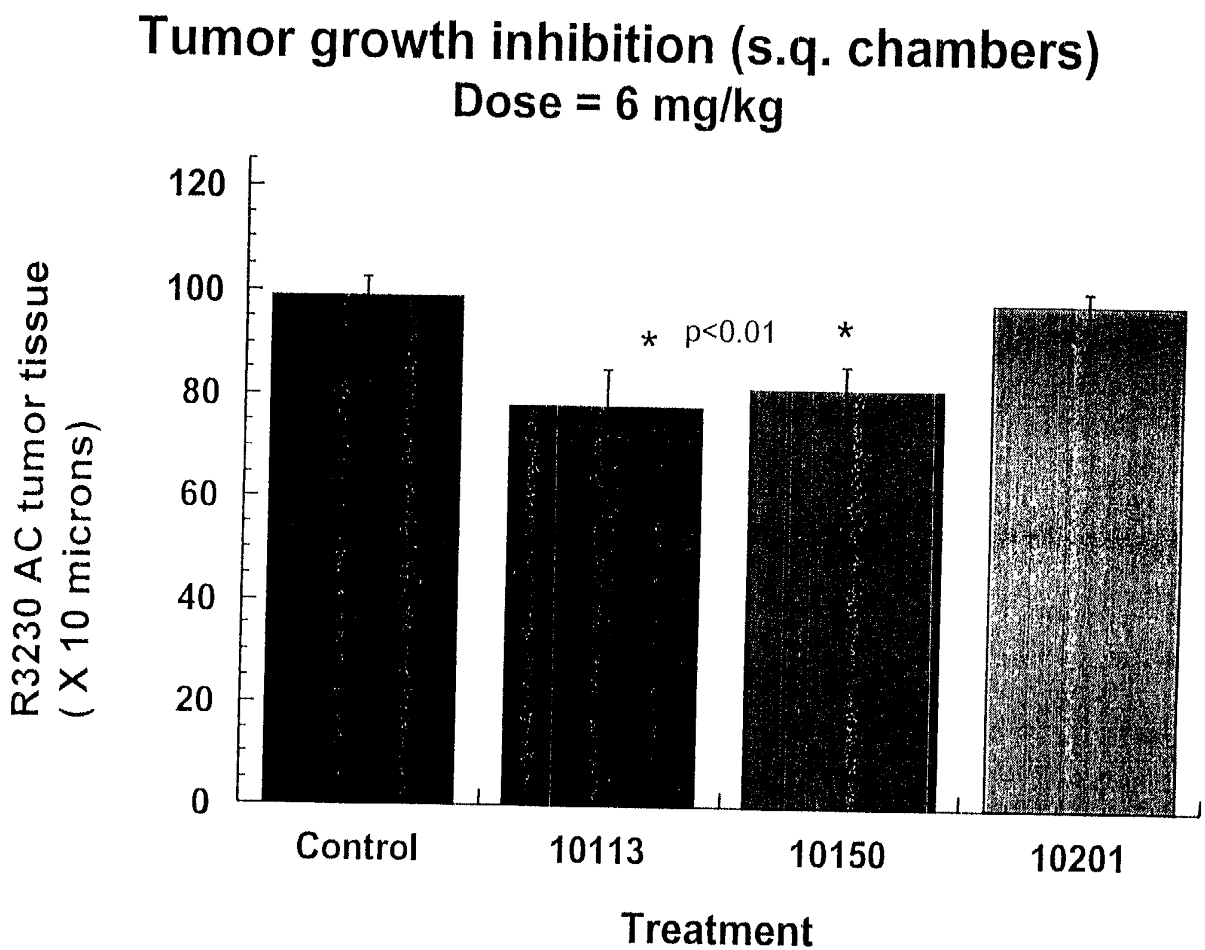


Figure 4



Tumor growth inhibition (s.q. chambers)
Dose = 6 mg/kg
R3230 AC tumor tissue
(X 10 microns)
120
100
80
60
40
20
0
* p<0.01 *
Control
10113
10150
10201
Treatment

Figure 5

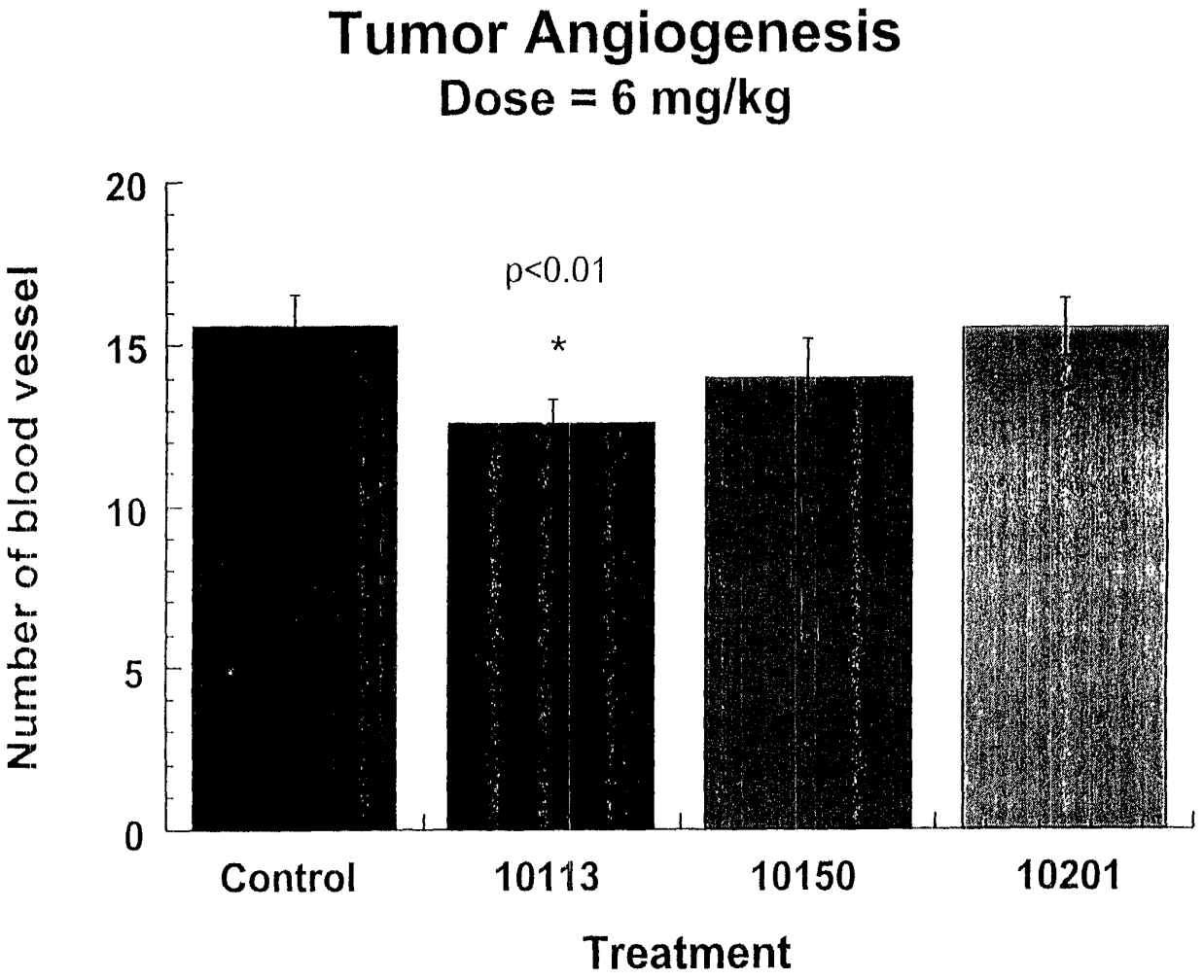
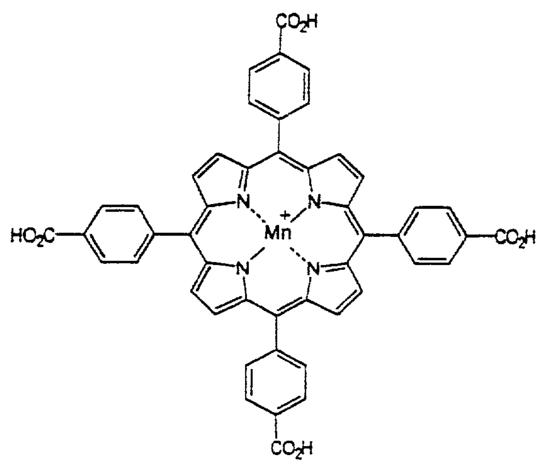

Tumor Angiogenesis
Dose = 6 mg/kg
Number of blood vessel
20
15
10
5
0
p<0.01
*
Control
10113
10150
10201
Treatment

Figure 6



Catalytic Antioxidant Metalloporphyrin
[MnTBAP]

Figure 7

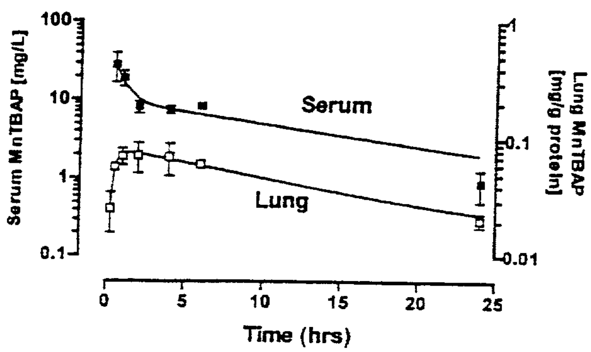


Figure 8

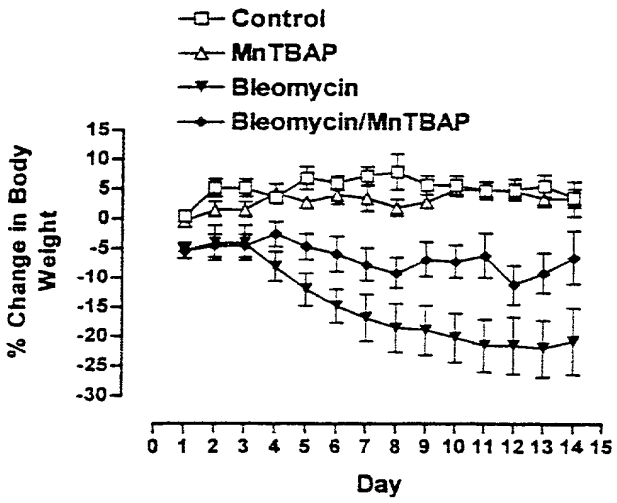

Control
MnTBAP
Bleomycin
Bleomycin/MnTBAP
% Change in Body Weight
15
10
5
0
-5
-10
-15
-20
-25
-30
0 1 2 3 4 5 6 7 8 9 10 11 12 13 14 15
Day

Figure 9

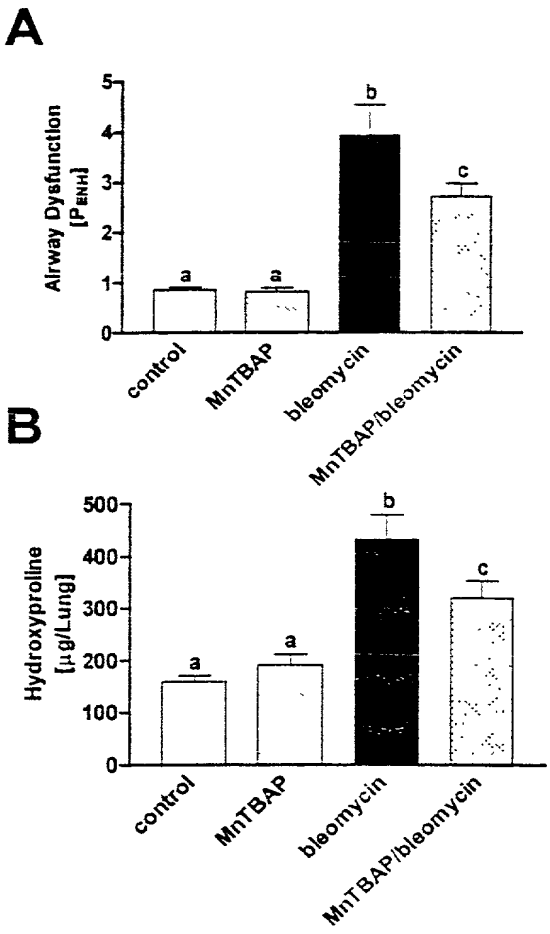

A
Airway Dysfunction [P_{ENH}]
5
4
3
2
1
0
a
a
b
c
control
MnTBAP
bleomycin
MnTBAP/bleomycin
B
Hydroxyproline [µg/Lung]
500
400
300
200
100
0
a
a
b
c
control
MnTBAP
bleomycin
MnTBAP/bleomycin

Figure 10

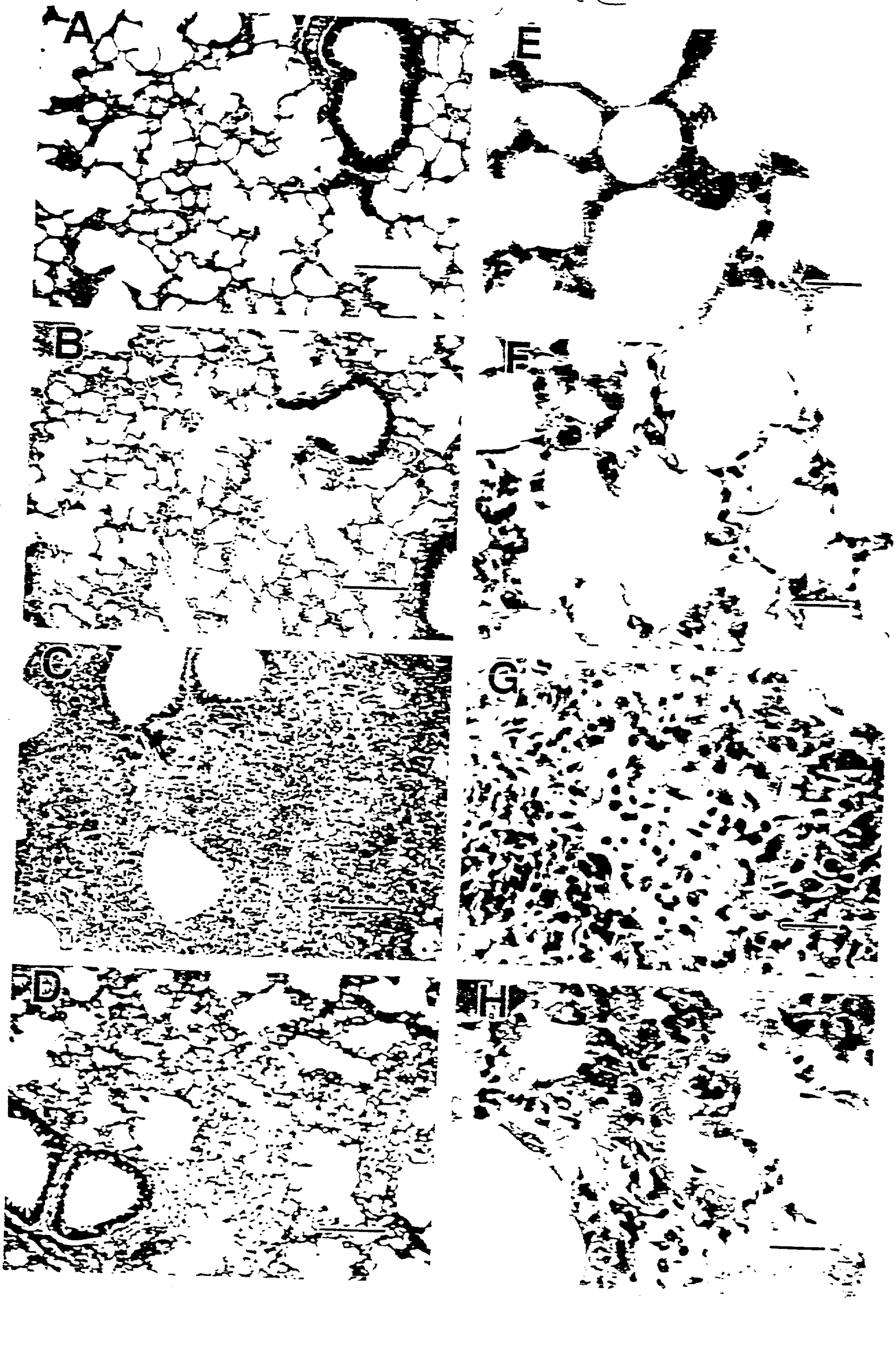


Figure 11

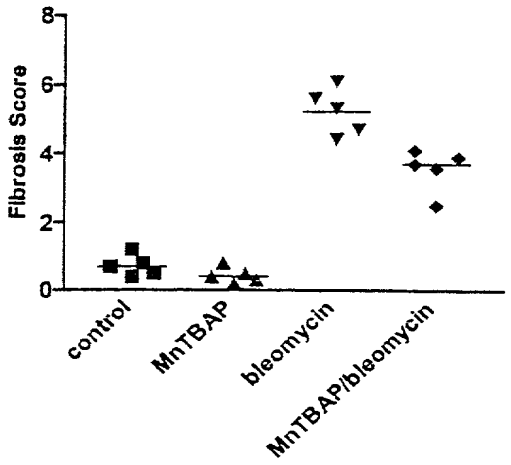


Figure 12

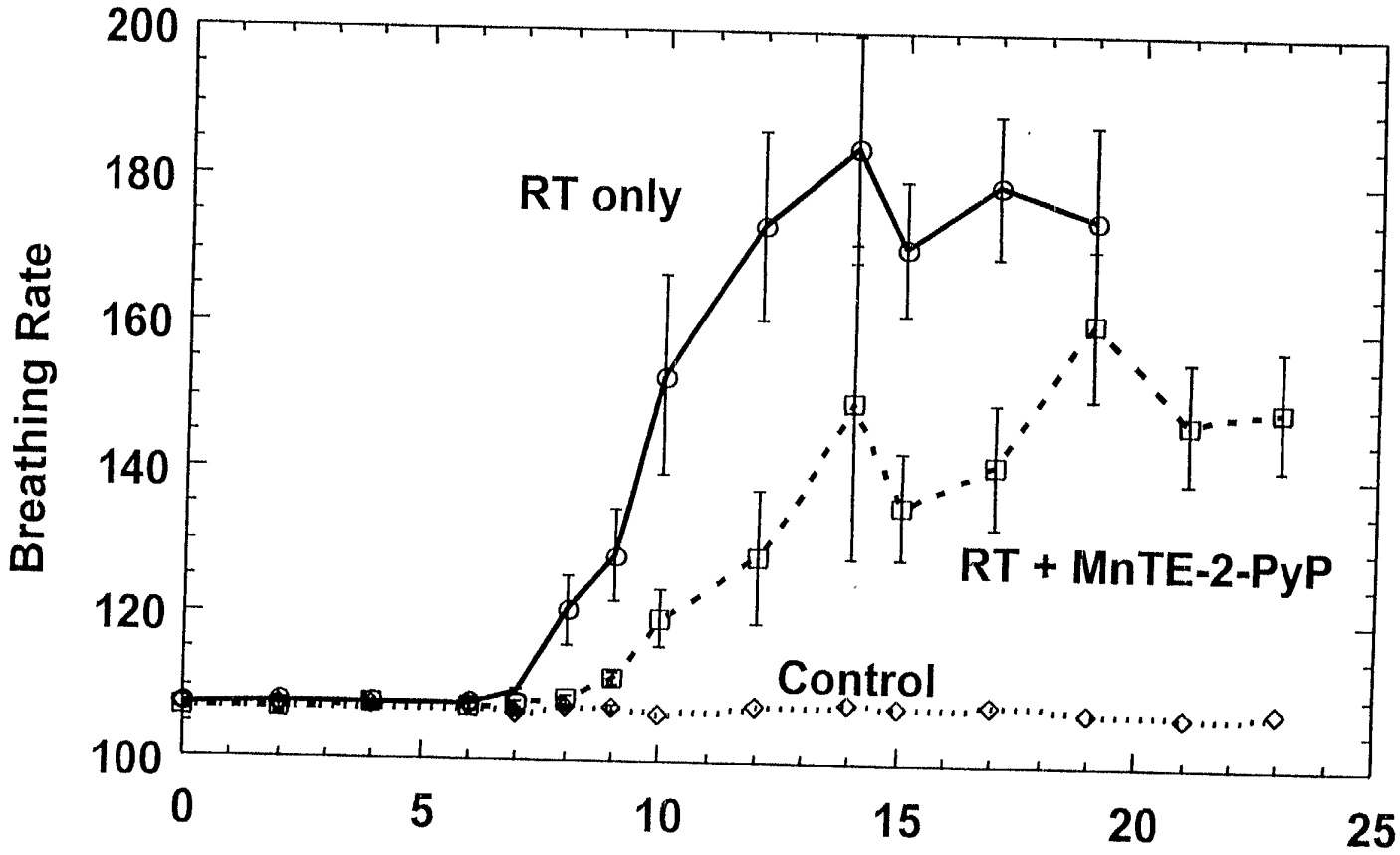


Figure 13A

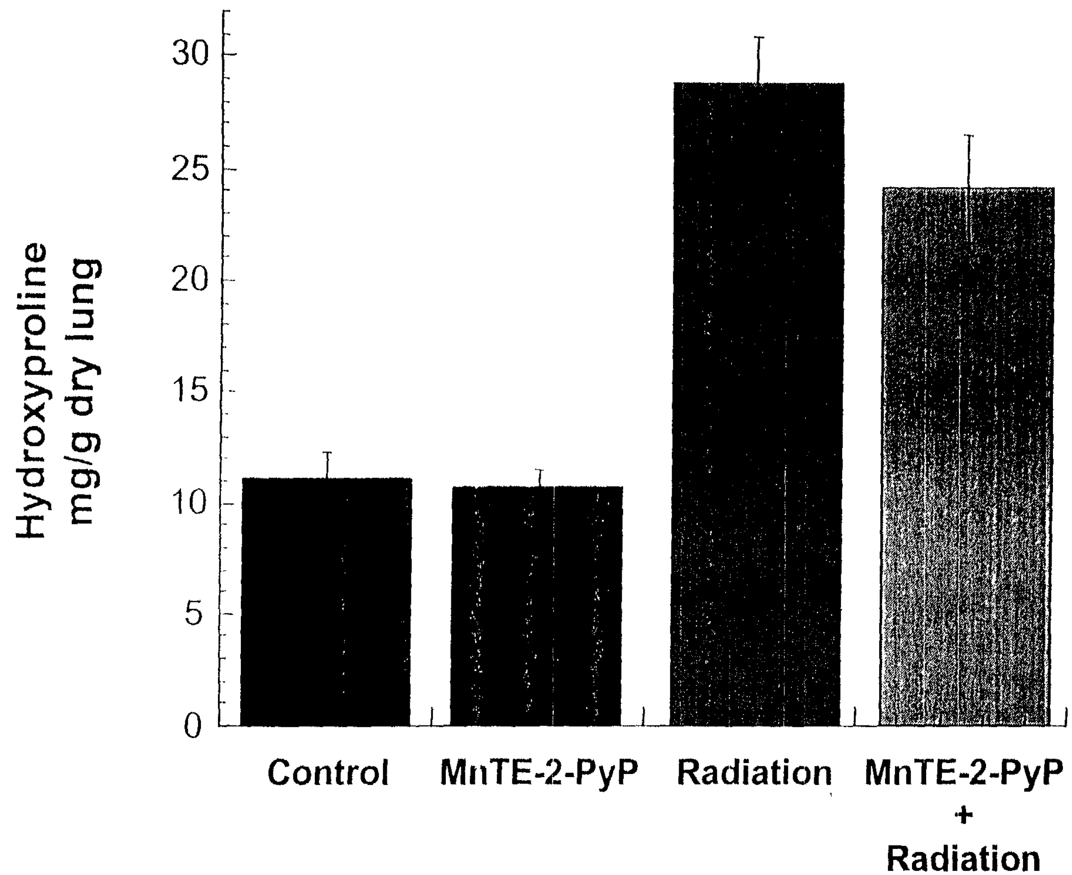

Hydroxyproline
mg/g dry lung
30
25
20
15
10
5
0
Control
MnTE-2-PyP
Radiation
MnTE-2-PyP
+
Radiation

Figure 13B

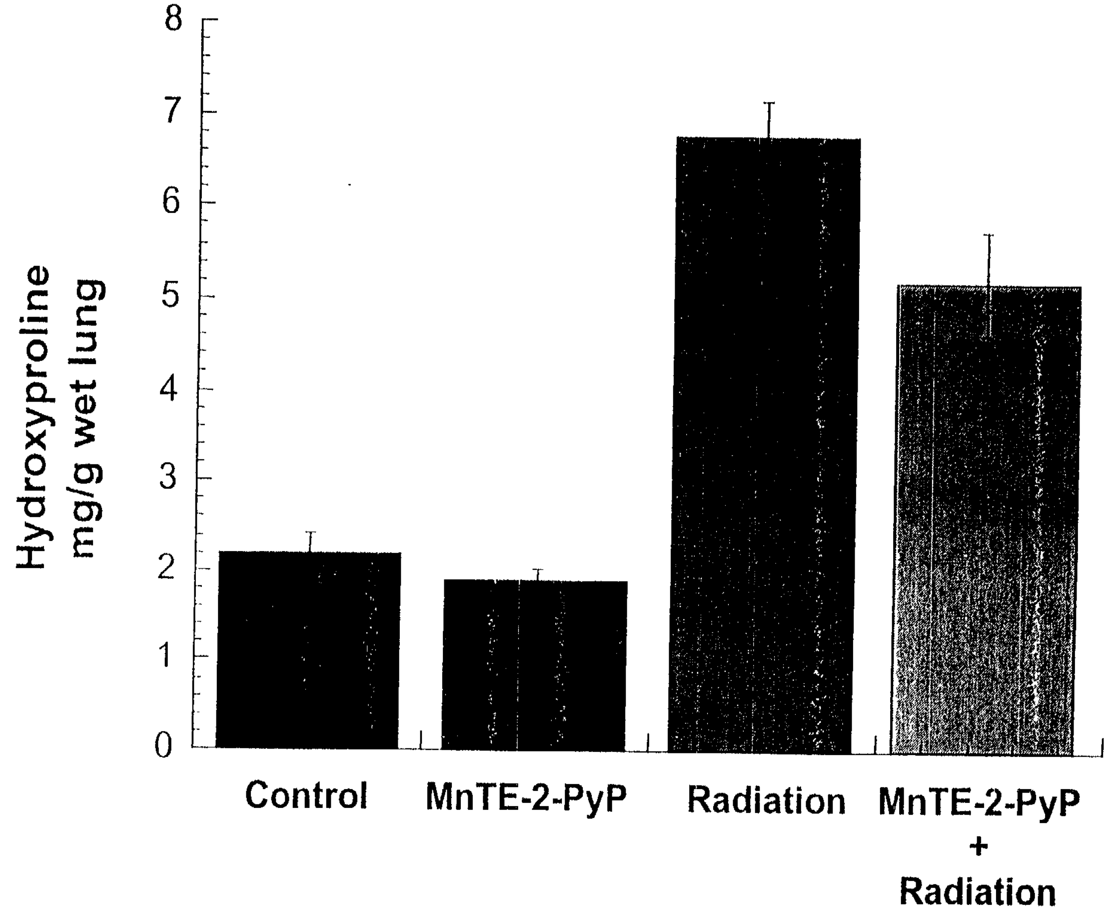
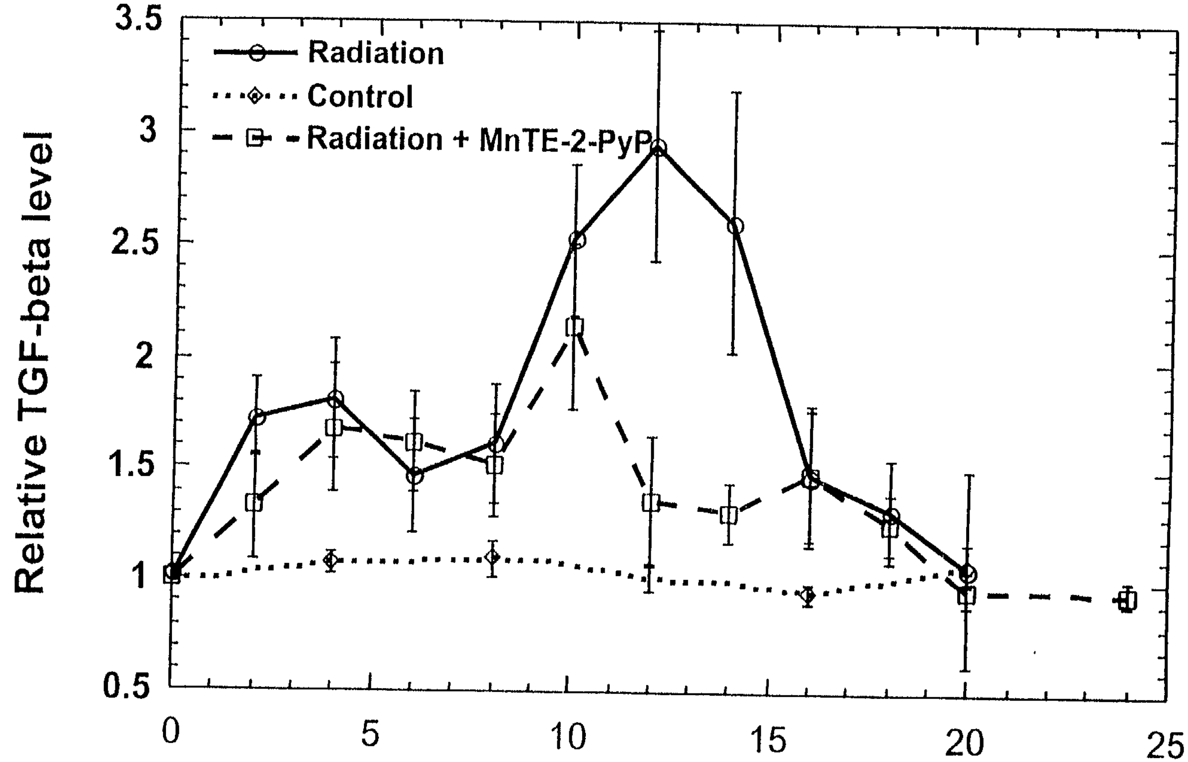


Figure 14



Radiation
Control
Radiation + MnTE-2-PyP
Relative TGF-beta level
3.5
3
2.5
2
1.5
1
0.5
0
5
10
15
20
25

Figure 15

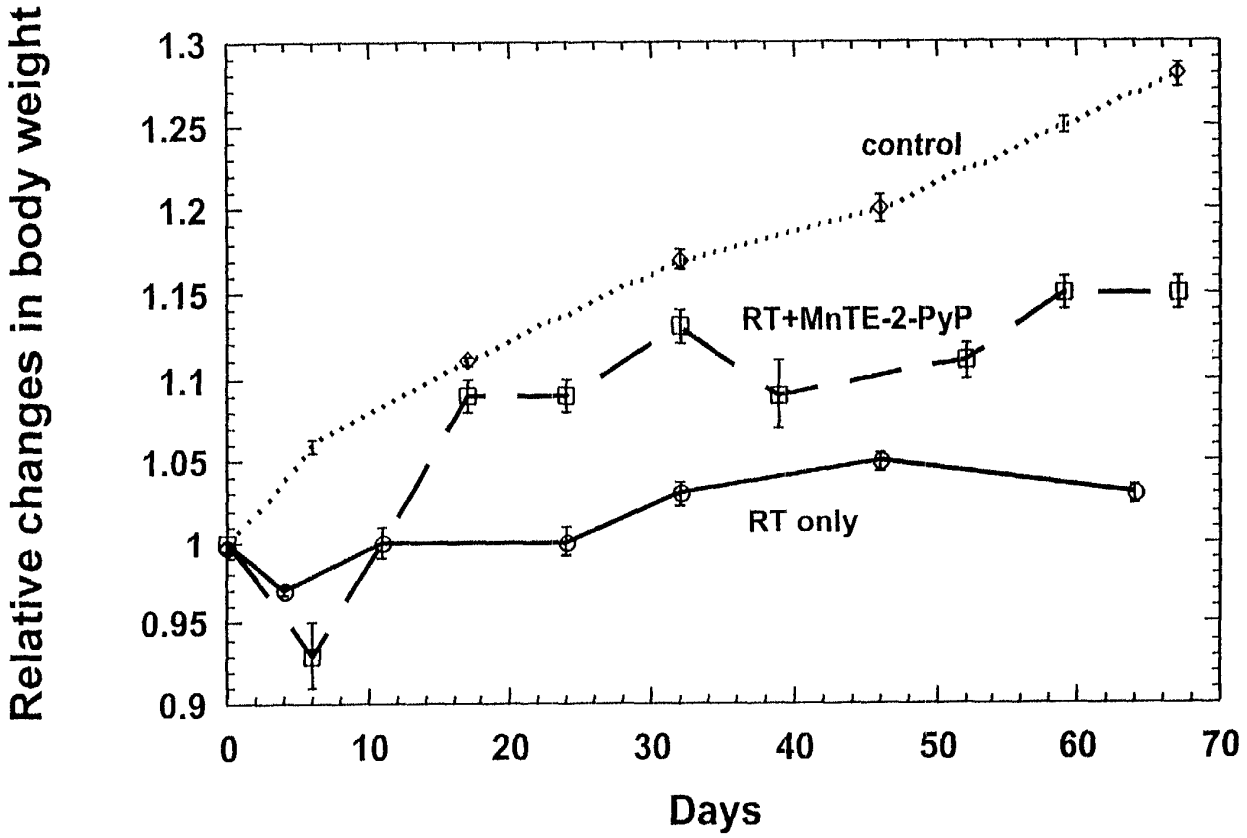


FIGURE 16

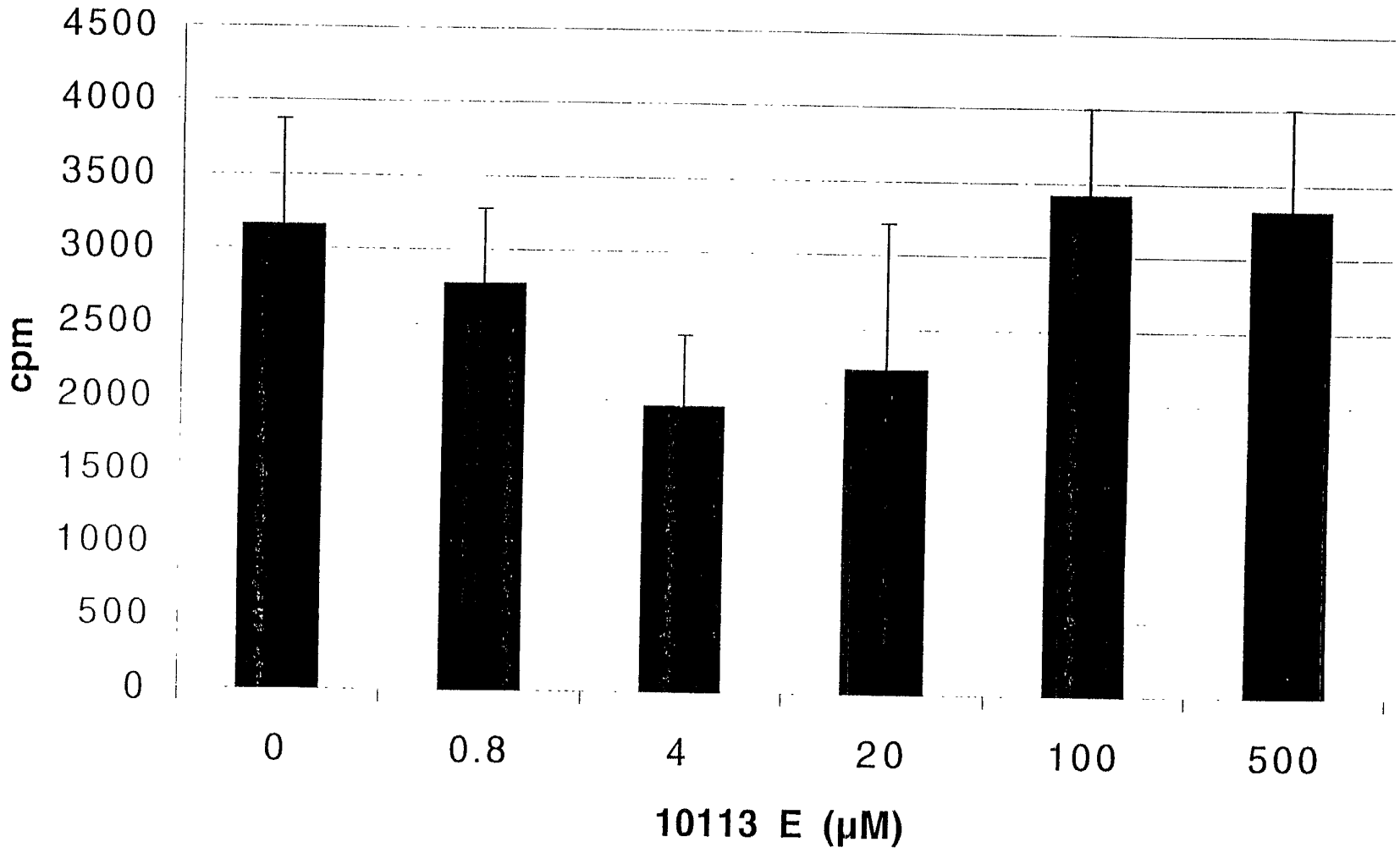
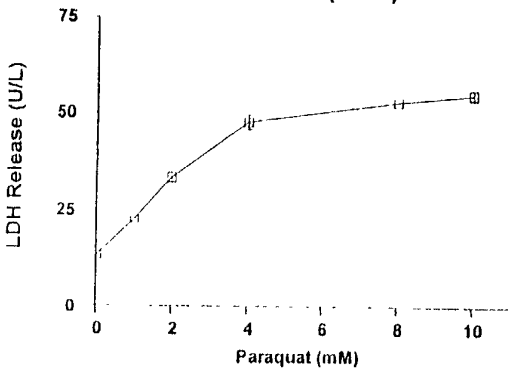
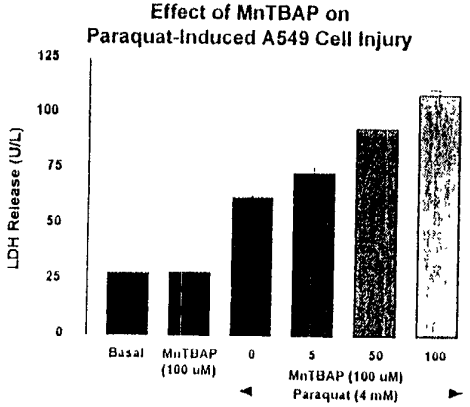

A549 3H-Thymidine uptake at 24 hours
4500
4000
3500
3000
2500
2000
1500
1000
500
0
cpm
0
0.8
4
20
100
500
10113 E (µM)

Figure 17

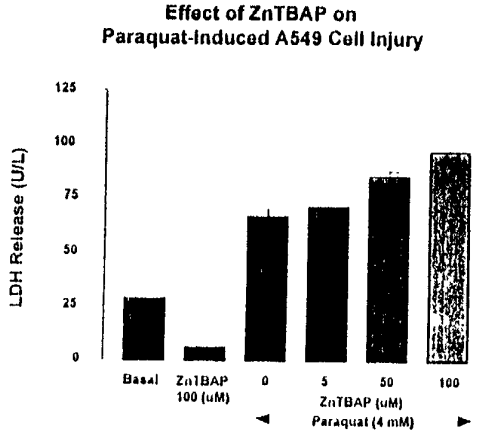
A



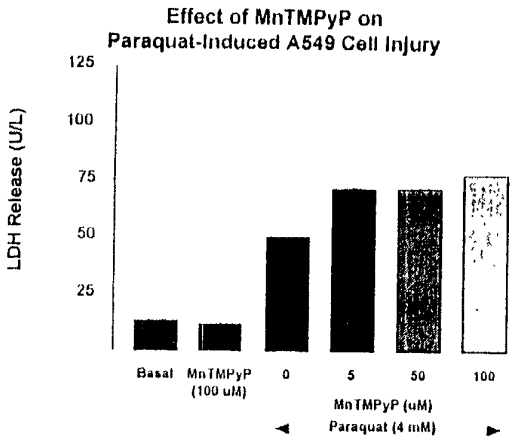
B



C



D



E

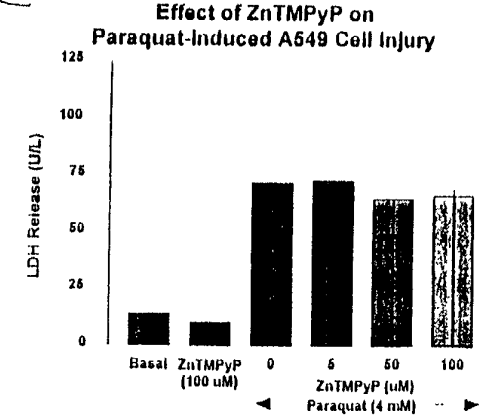


Figure 18

INC-01 Blinded Mucositis Scores

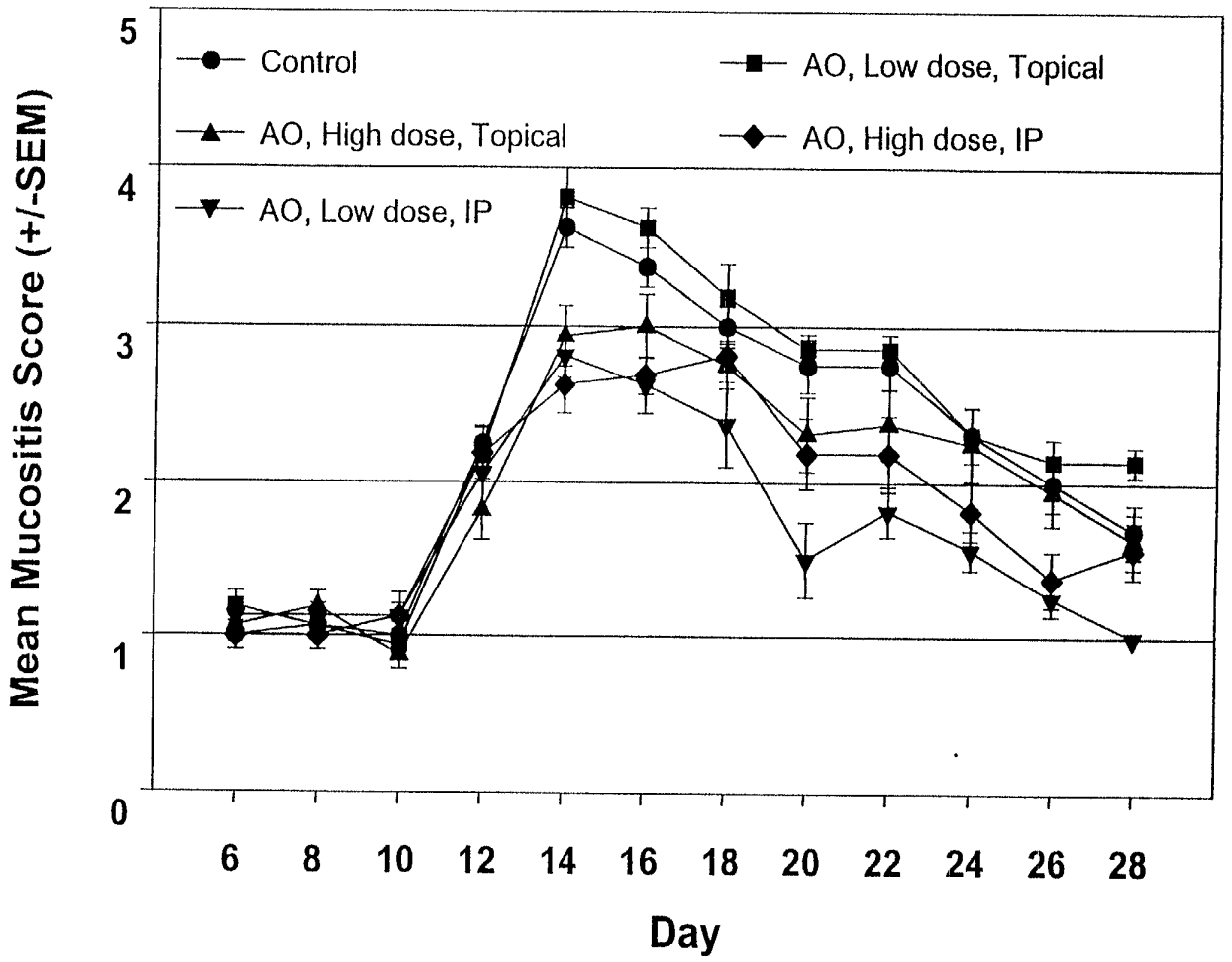


Figure 19